REMARKS

Favorable reconsideration of the subject application is respectfully requested in view of the amendments submitted herewith and the following remarks. Prior to entry of the Amendment submitted June 3, 2004, claims 1-29 and 31-57 were pending, and claims 1-14, 36-46, 53, 54, 56, and 57 were under consideration. According to the Amendment submitted June 3, 2004, claims 4, 8, 15-29, 31-35, 47-52 and 55 were cancelled, and claims 2, 9, and 10 were amended to more specifically describe certain embodiments of the invention and maintain proper dependency. With this Amendment, claims 1-3, 5-7, 9-14, 36-46, 53-54, and 56-57 have been cancelled without acquiescence to any rejection and without prejudice to further prosecution of the subject matter in a related divisional, continuation, or continuation-in-part application. New claims 58-71 have been added to more particularly point out certain subject matter encompassed by Applicants' invention. Support for these amendments is provided throughout the specification and in the claims as originally filed and does not, therefore, constitute new matter. Support for the new claims may be found in the specification, for example, at page 10, line 23 through page 12, line 1: page 13, lines 10-20; page 20, line 24 through page 21, line 2; page23, lines 5-6; page 26, lines 11-20; page 34, lines 11-16; page 39, line 4 through page 40, line 9; page 42, lines 14-22; page 47, lines 15-22; and page 50, lines 4-18.

Rejection Under 35 U.S.C. § 112, First Paragraph

Claim 57 stands rejected under 35 U.S.C. § 112, first paragraph, for allegedly containing new subject matter that was not described in the specification in such a way as to reasonably convey to the skilled artisan that the inventors had possession of the claimed subject matter at the time the application was filed. Specifically, the Action asserts that the recitation of antibodies or antibody parts bound to an array covalently or by first binding protein G to the array is not disclosed in the instant specification.

Applicants respectfully traverse this basis of rejection and submit that the claimed invention is described in the instant specification in sufficient detail such that a skilled artisan would appreciate that Applicants had possession of the invention as claimed. Applicants wish to point out that the subject matter recited in claim 57, which has been cancelled by the

Amendments submitted herewith, is recited in part in new claim 71. Claim 71 is directed in pertinent part to an assay device wherein the immunoglobulins are covalently bound to the array or wherein the immunoglobulins are bound to protein G that is first coated on the solid support. Support for covalent binding of immunoglobulins to the array is provided in the specification at page 26, line 21 through page 27, line 2. In addition, support for immunoglobulins being bound to the array by first coating protein G on the solid support followed by binding of antibodies to Protein G is provided in Example 1, at page 50, lines 11-18.

Thus, Applicants submit that present claim 71 is fully supported by the instant specification and does not constitute new matter, meeting the written description requirements under 35 U.S.C. § 112, first paragraph. Applicants therefore respectfully request that this rejection be withdrawn.

Rejection Under 35 U.S.C. § 112, Second Paragraph

Claims 4 and 8 stand rejected under 35 U.S.C. § 112, second paragraph, for allegedly being indefinite in their recitation of arrays of specific formulas to describe arrays of the invention. Specifically, the Action asserts that it is unclear whether the array is a mathematical representation of a rectangular arrangement of quantities or whether the array is a substrate for detecting biological interactions.

Without acquiescence to this basis of rejection and solely to expedite prosecution of the instant application, claims 4 and 8 were cancelled in the Amendment and Response submitted June 3, 2004, thereby rendering this rejection moot. Applicants respectfully request that this rejection be withdrawn.

Rejection Under 35 U.S.C. § 102(b)

Claims 1-4, 6-8, 14, 36-42, and 45 stand rejected under 35 U.S.C. § 102(b) for allegedly being anticipated by Clackson et al. (*Nature* 352:624-28 (1991)). Specifically, the Action asserts that Clackson et al. disclose an ELISA device comprising a combinatorial library of rearranged heavy and light chains arranged in a matrix, wherein binding is judged by a variable signal and is indicative of a condition.

Applicants respectfully traverse this basis of rejection and submit that the claimed invention is not anticipated by Clackson et al. As an initial matter, Applicants note that claims 4 and 8 were cancelled in the Amendment and Response submitted June 3, 2004, without acquiescence to this rejection. Applicants submit that in view of the Amendments submitted herewith, which include cancellation of claims 1-4, 6-8, 14, 36-42, and 45 without prejudice and without acquiescence to this rejection, the rejection of these claims is rendered moot. Applicants further submit that Clackson et al. fail to anticipate the subject matter recited new claims 58-71.

Applicants submit that Clackson et al. fail to anticipate the present claims because the document fails to teach or suggest each and every limitation of the claims (*see, e.g., Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987) ("A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference."); M.P.E.P § 2131). Specifically, Applicants submit that Clackson et al. fail to teach an assay device for determining the presence of cancer or a propensity to develop cancer in an animal or for determining the presence of a disease or disorder of the immune system, wherein the assay device comprises an array of immunoglobulin molecules that are immobilized to discrete regions on a solid surface and that specifically bind to different cell surface antigens. Furthermore, Clackson et al. fail to teach or suggest that the array comprises a plurality of different immunoglobulin molecules, wherein each immunoglobulin is capable of interacting with a biological sample that comprises a cell expressing the respective cell surface antigen to which the antibody specifically binds. Clackson et al. also fail to describe an assay device as recited wherein interaction between the immunoglobulin molecules and their respective cell surface antigens establishes concurrently a discriminatory image of antigen expression that indicates the presence of a disease state.

For reasons articulated in the Amendment and Response submitted to the PTO on June 3, 2004, Applicants respectfully disagree with the assertion in the Action that Clackson et al. teach or suggest an ELISA device that comprises a combinatorial library of rearranged heavy and light chains arranged in a matrix, wherein binding is judged by a variable signal and is indicative of a condition. Applicants submit that Clackson et al. describe the use of the art-known ELISA immunoassay method in which a single antigen, the hapten phOx, is bound to an

immunoassay plate, which is used for screening phage display libraries to identify phage with a phage coat protein fused to single chain Fv antibody fragments that specifically bind phOx. Subsequent to the ELISA and independent of any ELISA device, the polynucleotides encoding the antibody fragments identified in the ELISA are then sequenced and translated to provide the amino acid sequence of the variable regions of the heavy and light chains of the single chain Fv antibody fragments. Applicants further submit that Clackson et al. fail to teach or suggest that selection of anti-phOx antibody fragments by the method disclosed therein is indicative of any disease state or condition. Thus, the cited document teaches an assay for detecting antibody fragments with specificity for a single antigen, in contrast to Applicants' claimed invention in which the interaction of a plurality of immobilized immunoglobulin molecules specific for different cell surface antigens establishes concurrently a discriminatory image of antigen expression that is indicative of a disease or condition as recited.

Accordingly, Applicants respectfully submit that the claimed assay device meets the requirements for novelty under 35 U.S.C. § 102 and request that this rejection be withdrawn.

Rejection Under 35 U.S.C. § 103

Claims 1-14, 36-46, 53, 54, and 56 stand rejected under 35 U.S.C. § 103(a), as allegedly being obvious over Clackson et al. taken with Marks et al. (*J. Mol. Biol.* 222:581-97 (1991)) in view of Gallo et al. (U.S. Patent No. 5,968,513). Specifically, the Action asserts that Clackson et al. provide the teachings described above in the context of the novelty rejection but concedes that Clackson et al. fail to disclose labeled antibodies as recited in claims 53 and 54 or the further limitations described in claims 5, 9-13, and 43-46. The Action asserts that Marks et al. disclose the use of labeled antibodies and that Gallo et al. describe methods of treatment of cancer using monoclonal antibodies capable of binding cell surface determinants. The Action concludes that the skilled artisan would have been motivated by the improvements of Marks et al. to improve on the method of treatment of diseases caused by pathogens as taught by Gallo et al. by using antibodies with greater diversity and strong binding as taught by Clark et al. [*sic*, Clackson et al.?].

Applicants traverse this rejection and submit that the Action fails to establish a *prima facie* case of obviousness because the cited references fail to teach or suggest each

element of the claimed invention, which is required in order for the PTO to establish a *prima facie* case of obviousness. *In re Royka*, 490 F.2d 981 (CCPA 1974). Applicants submit that the PTO has also failed to show that the cited documents provide any teaching, suggestion, or motivation to combine or modify the teachings of the prior art to produce the claimed invention, and has also failed to show that the combined teachings of the references indicate that when the references are combined, a person having ordinary skill in the art will achieve the claimed invention with a reasonable expectation of success.

Applicants note that claims 4 and 8 were cancelled in the Amendment and Response submitted June 3, 2004, without acquiescence to this rejection. Applicants submit that in view of the Amendments submitted herewith, which include cancellation of claims 1-4, 6-8, 14, 36-42, and 45 without prejudice or acquiescence, the rejection of these claims is rendered moot. Applicants further submit that a person having ordinary skill in the art would not find it obvious to combine the teachings of Clackson et al. with Marks in view of Gallo et al. to achieve Applicants' invention as recited in new claims 58-71 with any expectation of success.

Applicants submit that the subject matter of the instant claims is not obvious in light of Clackson et al., Marks et al., and Gallo et al., each alone or in any combination, because none of these documents teaches an assay device for determining the presence of cancer or a propensity to develop cancer in an animal or for determining the presence of a disease or disorder of the immune system, wherein the assay device comprises an array of immunoglobulin molecules that are immobilized to discrete regions on a solid surface and that specifically bind to different cell surface antigens. Each document alone or in combination also fails to teach or suggest that wherein each immunoglobulin of the array is capable of interacting with a biological sample that comprises a cell expressing the respective cell surface antigen, the interaction between each immunoglobulin molecule and its respective cell surface antigen establishes concurrently a discriminatory image of antigen expression, which is a differential pattern of density that provides an identifiable signal indicative of the presence of the disease or condition.

As discussed in detail above (please see arguments rebutting the novelty rejection), Clackson et al. fail to teach or suggest each and every limitation of the claimed assay device and merely teach a well-known ELISA immunoassay method for detecting antibody fragments (scFv) that bind to a single hapten antigen. Neither the teachings in Marks et al. nor

Gallo et al. remedy the deficiencies of Clackson et al. The Action asserts that Marks et al. teach the use of peroxidase-labeled antibodies for detecting binding of an antibody to lysozyme. Applicants submit that Marks et al. provide nothing more than a general reference for using labeled antibodies, a technique well known to persons skilled in the immunodetection art. Gallo et al., alone or in combination with either Clackson et al. or Marks et al. or both documents, also fail to teach or suggest each element of the presently claimed assay device. Gallo et al. teach art known methods for separation or isolation of particular cell types using antibodies specific for cell surface antigens, but fail to teach or suggest an assay device comprising an array of immunoglobulins for use in detecting a disease or disease condition such as cancer or an immune disorder.

For reasons already made of record in the Amendment and Response submitted to the PTO on June 3, 2004, Applicants are puzzled by the statements in the Action regarding alleged teachings in Marks et al. and Gallo et al. that relate to a method of treatment of cancer and immunological disorders. Applicants respectfully point out that the present claims are directed to an assay device comprising an array of immunoglobulin molecules, which bind to their cognate binding partners in a sample to produce a discriminatory image of antigen expression that is indicative of a particular disease or disease condition. Accordingly, the skilled artisan would appreciate that the claimed invention may be used in the detection of a disease. In contrast, the arguments provided in the Action as allegedly demonstrating obviousness of the claimed invention appear largely directed to methods of treating disease although the cited references do not appear to provide such teachings. Applicants submit that such teachings are inapposite to the patentability of the claimed assay device.

The Action cites Gallo et al. as disclosing a treatment for cancer and immunological disorders. However, Applicants note again that that the present claims are directed to an assay device comprising an array of molecules and are not, in fact, directed to methods of treatment. While Gallo et al. describe specific methods of separating out cells of interest using antibodies directed to cell surface markers, Gallo et al. makes absolutely no reference to any specific patterns of markers being indicative of a condition.

The cited references clearly fail to teach each element of the claimed invention. Furthermore, the Action fails to establish any teaching, suggestion, motivation, or desirability to

combine the cited documents to achieve the Applicants' invention. When claims are rejected for being obvious over a combination of prior art references, something in the prior art as a whole must suggest the desirability, thus the obviousness, of making the combination (*see In re Rouffet*, 149 F.3d 1350, 1355, 47 U.S.P.Q.2d 1453 (Fed. Cir. 1998)).

In the present case, none of the cited documents teaches, suggests, or provides any motivation to the skilled artisan to combine the teachings therein to achieve Applicants' claimed assay device. Contrary to the Action's stated reasoning, Marks et al. is not related to a general method of treatment but instead describes a method for identifying and isolating human antibodies from phage libraries and, therefore, provides no basis for the Action's argument that improvements in a method of treatment described by Marks et al. would be applicable to treatment of a disease as described by Gallo et al. Moreover, as discussed above, any combination of teachings in the cited document related to methods of treatment is irrelevant to the nonobviousness of the presently claimed subject matter. Accordingly, any rejection relying on this combination of teachings in the cited documents, which combination appears irrelevant to the subject matter recited in the present claims, fails to meet the requirements for establishing a *prima facie* case of obviousness.

Accordingly, Applicants respectfully submit that the present claims satisfy the requirement for nonobviousness under 35 U.S.C. § 103. Applicants therefore respectfully request that this rejection be withdrawn.

Applicants respectfully submit that all claims in the application are allowable. Favorable consideration and a Notice of Allowance are earnestly solicited. In the event that the Examiner believes a teleconference will facilitate prosecution of this case, the Examiner is invited to telephone the undersigned at 206-622-4900.

Respectfully submitted,

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